REMARKS

Claims 1-12, 29-32, 35 and 40-45 were previously pending in this application. By way of this amendment, claims 1-11, 29-32 and 40-45 have been amended. Claims 13-28, 33-34 and 36-39 were previously cancelled. Claims 9, 12 and 35 were previously presented or original claims. Upon entry of this amendment, claims 1-12, 29-32, 35 and 40-45 remain pending in this application. No new matter has been added.

The claims have been generally amended to more specifically specify the particular structural features of the LXRβ crystals disclosed in the instant application, for example, in Table 1, in paragraphs 18-20 and 125 of US 07/0060740.

The claim amendments and cancellations made herein have been made solely to expedite prosecution of the instant application. Applicants reserve the right to prosecute these claims in other applications.

Applicants note with appreciation the Examiner's reconsideration and withdrawal of previous objections to the specification and rejections of the claims under 35 U.S.C. § 112, second paragraph.

Claim Objections

On pages 4-5 of the Office Action, the Office has objected to the claims because of certain informalities. Each of the these objections is addressed individually below:

a) Claims 1, 6, 29, 40 and 44 were objected to for containing a misspelling in "3-(3-(2-chloro-3-**tru**fluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid." This objection has been obviated by amending claims 1, 6, 29, 40 and 44 (as well as claims depending therefrom) to recite the corrected spelling for this ligand, as suggested by the Examiner.

b) Claims 4, 5, and 7 were objected to because the recitation of "wherein said crystal belongs to space group …". This objection has been obviated by amending the claims to recite remove the phrase objected to by the Office.

c) Claims 10 and 40 are objected to because of the recitation of "NR box of TIF2." This objection has been obviated by amending the claims to recited the full name of "Nuclear Receptor (NR) box 1 of Transcription Intermediary Factor 2."

d) The objection to claims 29 and 30 have been obviated by correcting the typographical errors.

e) Claim 31 was objected to because the recitation of "in Figure 5a (SEQ ID NO: 1)" and "in Figure 5b (SEQ ID NO: 2)". This objection has been obviated by amending the pending claims to replace this phrase with "as set forth in" the appropriate sequence identifier, as suggested by the Office.

f) The objection to claim 42 has been overcome by inserting the missing "angstrom" symbols after each unit cell dimensions, a, b and c.

In view of the amendments and arguments made herein, the claim objections are now moot. Reconsideration and withdrawal of the claim objections is respectfully requested.

Rejection of Claims 1-12, 29-32, 25, and 40-45 under 35 U.S.C. §112, Second Paragraph

On pages 5-8 of the Office Action, the Office has rejected claims 1-12, 29-32, 35, 40-45 as allegedly being indefinite under 35 U.S.C. §112, second paragraph. Each aspect of this rejection is addressed individually below.

a) Claims 1, 2, 8-10, 29, 30, 40-42, 44 and 45 (4-7, 11, 12, 35 and 43 dependent therefrom) were rejected because the Office considered the phrase, "LXRβ ligand binding domain" or "LBD," to be allegedly unclear and indefinite.

While Applicants do not concede to any aspect of the Office's stated reasons for this rejection, this rejection has been met by amending the rejected claims remove the phrase "an amino acid sequence having at least 95% sequence homology to the Leu220 to Glu461 of human LXRβ ligand binding domain" from claims 1 and 40, and "a homologue of said molecule or molecular complex" from claims 29, 30, 44 and 45. It is noted that the amended claims explicitly refer to the "LXRβ ligand binding domain" as a domain comprising or consisting of the amino acid sequence from Leu220 to Glu461 of SEQ ID NO:1. The fact that some degree of deviation from the amino acid specified (*i.e.*, at least 95% homology to the amino acid sequence specified) was permissible in claims 1 and 40, or claims 29, 30, 44 and 45 still allow for a limited structural deviation of no more than 1.5 Å does not render the recitation of "LXRβ ligand binding domain" in the claims indefinite. It simply means that the claims encompass the specified variants of the amino acid sequences or the recited range of deviation from the

structural coordinates of Table 2. The LXRβ amino acid sequence and domain structure were known in the art prior to the present application (*see e.g.*, paragraphs 3 and 121 of US 07/0060740) and is disclosed in the instant specification as SEQ ID NO:1. Thus, the skilled artisan would have understood what was mean by the term "LXRβ ligand binding domain" or "LBD" in view of the teachings of the specification and the art at the time. Accordingly, Applicants submit that the term "LXRβ ligand binding domain" is clear and definite.

In another aspect of this rejection, on pages 7-8 of the Office Action, the Office has rejected claims 1, 7, 32 and 40, and claims dependent therefrom as being allegedly unclear on several grounds. This aspect of the rejection has been met by amending these claims to clarify the objections noted by the Office.

In yet another aspect of this rejection, the Office rejected claim 43 as being allegedly indefinite by stating that "[i]t is unclear how a crystal/crystal complex can be resolved by an *in silico* method." This aspect of the rejection has been met by amending claim 43 to specify that it is the structural coordinates of the binding pocket (and not the crystal complex) according to base claims 29 or 30 that was resolved by molecular replacements using the structure of the thyroid hormone receptor as a search model. Applicants request the Examiner to reconsider the position that this limitation was not deemed to impart patentable weight to claim 43, as it distinguishes the structural coordinate information recited in the present claims from the coordinate information disclosed by Bledsoe *et al.* in USSN 10/418,007 (published as US 04/0018560), which was resolved using the structure of the retinoid acid receptor gamma as the search model.

In view of the amendments and arguments made herein, Applicants submit that the rejection of the claims is now obviated. Reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

Rejection of Claims 1-12, 29, 30 and 40-45 under 35 U.S.C. § 112, First Paragraph

New Matter Rejection

On pages 9-10 of the Office Action, the Office has rejected claims 1-12, 29, 30 and 40-45 as allegedly containing new matter. Each of the grounds for this rejection is addressed individually below.

Claim 1 was rejected because of the recitation of phrase "a polypeptide comprising an amino acid sequence at least 95% identical to the sequence from Leu220 to Glu461." While Applicants do not concede to any aspect of the Office's stated reasons for this rejection, this aspect of the rejection has been met deleting this phrase from the pending claims.

With respect to the rejection of claims 6 and 7 reciting the particular ligand and crystal space group and unit cell dimension, Applicants submit that claims 6 and 7, as amended herein, are explicitly disclosed in paragraph 20 and 19, respectively, of US 07/0060740. Thus, amended claims 6 and 7 do not contain new matter.

In view of the amendments made herein, Applicants submit that the rejection of the claims as allegedly containing new matter is now obviated.

Written Description

On pages 11-16 of the outstanding Office Action, the Office has rejected claims 1-12, 29, 30 and 40-45 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

In maintaining this rejection, the Office acknowledges that the specification describes four x-ray diffraction quality crystals (two crystals with space group $P2_12_12_1$, one crystal with space group $P6_122$ and one crystal with space group $P2_12_12$) having the specific amino acid sequence, space group, unit cell dimension and bond angles as disclosed in pages 6 and 24, and Table 1. However, the Office states that "[i]n light of the notion that obtaining X-ray diffraction quality crystals is highly unpredictable" (citing to the previous enablement rejection), "the genera of crystals [*e.g.*, having additional amino acid sequences attached] is not adequately described in the instant application." (Office Action, at page 16).

The rejection has been met in part and is traversed to the extent that it is applied to the newly amended claims. It is noted that the relevant standard articulated by the Federal Circuit to comply with the written description requirement in cases involving genus/species is whether a genus is described by disclosing (1) a representative number of species within that genus; or (2) its "relevant identifying characteristics," such as "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo*

Biochem, Inc v. GenProbe Inc., 323 F.3d, 956, 964 (Fed. Cir. 2002). This standard is reiterated in the "Revised Interim Guidelines for Examination of Patent Applications Under 35 U.S.C. 112," where it provides that "[s]atisfactory disclosure of a "representative number" [of species] depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." 66 FR 1099, 1106 (emphasis added), Moreover, the Office is reminded that "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *Id.* (emphasis added) For the reasons explained in more detail below, Applicants submit that the claims, as presently amended, comply with the written description requirements.

Claims 8-10 (and claims dependent therefrom) are directed to crystals of the LXRβ LBD, in apo- (unliganded) form or complexed to the particular ligand specified, having the *exact* space group and unit cell dimensions disclosed in the instant specification, *e.g.*, in paragraphs 18-20, respectively, of US 07/0060740. Similarly, dependent claims 3-7 and 42 are directed to crystals of the LXRβ LBD, in apo form or complexed to the particular ligand specified, that comprise or consist of the particular amino acid sequence of the LXRβ LBD specified, and recite the *exact* space group and unit cell dimensions disclosed in the instant specification, *e.g.*, in Table 1, paragraphs 125, 20 and 19, respectively, of US 07/0060740. Paragraphs 122-126 of US 07/0060740 describe experimental data with explanations on how to make and characterization of the claimed crystals.

The scope of the genus encompassed by claims 3-10 and 42 (and its dependencies) is commensurate with the LXRβ LBD crystal species disclosed by the Applicants. The recitation of the exact space group and unit cell dimensions in these claims provide ample structural features in common to support the breadth of the claims. It is undisputed that claims 3-10 and 42 in their present form impose almost identical structural parameters as those specified by hypothetical claim 1 exemplified in case 4 of the "Trilateral Project WM4 Comparative Studies in New Technologies: Report on Comparative Study on Protein 3-Dimensional (3-D) Structure Related Claims" released in November 2002 ("the Trilateral Report"). The USPTO indicated in the Trilateral Report that hypothetical claim 1 would meet the written description requirement

because the crystal structure of the protein is provided in the claim by specifying the cell unit dimension. More specifically, claim 1 in case 4 of the Trilateral Report is directed to a crystalline form of a known protein P, and reads as follows: "A crystalline form of protein P having unit cell dimensions of a=4.0nm, b=7.8nm, and c=11.0nm." At pages 8 and 66 of the report, the hypothetical specification of case 4 is described as including, *inter alia*, that the inventors have newly produced a stable crystalline form of protein P and that the description gives experimental data with explanations of how to make the crystals. The Trilateral Report, at page 67, referring to the claim of case 4, states that "the claim complies with the written description requirement because the *structure* of protein P is provided." (emphasis added).

Like the hypothetical claim 1 presented in case 4 of the Trilateral Report, claims 3-10 and 42 are directed to a crystalline form of a specific known protein (*i.e.*, LXRβ LBD), which was characterized in the art prior to the filing date in terms of its structure and function. Also similar to the hypothetical claim 1 presented in case 4, instant claims 3-10 recite the unit cell dimensions of the crystal. The present specification discloses, *inter alia*, that the inventors had newly produced six crystalline forms of LXRβ LBD, provided LXRβ LBD sequence and ligand structural information, experimental data with explanations on how to make the crystals, and the three-dimensional structure of a crystalline form of the LXRβ LBD polypeptide (*see* specification at, *e.g.*, paragraphs 17-21, 117-126 (including Table 1 and Figures 5a-7 of US 07/0060740). Applicants clarify that at least the following species of LXRβ LBD, in apo or complexed form, were disclosed in the instant application as filed: 2 species of crystals of LXRβ LBD complexed with T0901317 or GW3965 having space group $P2_12_12_1$ are disclosed in Table 1 of US 07/0060740; 2 species of crystals of LXRβ LBD in apo form or complexed with T0901317 having space group $P6_122$ are disclosed in paragraph 19 and 125, respectively, of US 07/0060740; 2 species of crystals of LXRβ LBD in apo form or complexed with the NR-box of TIF having space group $P2_12_12$ are disclosed in paragraphs 18 and 20, respectively, of US 07/0060740. Thus, Applicants respectfully submit that for at least the reasons set forth above, the specification amply provides written description for the crystalline forms of LXRβ LBD polypeptide as presently set forth in claims 3-10 and 42.

The remaining claims also comply with the written description requirement. For example, claims 1 and 40 require the LXRβ LBD crystal to be complexed to a particular ligand

and to have the space group specified (namely, $P2_12_12_1$, $P6_122$ and $P2_12_12$), in addition to the LXRβ LBD amino acid sequence specified. Claims 2 and 41 are directed to LXRβ LBD crystals having the structural parameters of the base claim, wherein the LXRβ LBD polypeptide sequence "consists of" the amino acid sequence disclosed in SEQ ID NO:1. Similarly, claims 29-30 and 43-45 require the LXRβ LBD crystal to be complexed to a particular ligand and to include the binding pocket having the structural coordinates of Table 2 within the deviation specified, in addition to the LXRβ LBD amino acid sequence specified. Therefore, these claims specify sufficient common attributes of the claims crystals, in terms of space groups, structural coordinates and LXRβ LBD amino acid sequence to be fully supported by the six members of the genus of LXRβ LBD crystals disclosed by the Applicants. The Office is reminded that a description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces.

In sum, the scope of the aforementioned genus encompassed by the claims does not have substantial variation in view of the claims' precise structural parameters specified by the claims. Given the defined scope of the claims, Applicants respectfully submit that the specification provides ample number of species having a common attribute to show that the applicants were in possession of the claimed crystals and methods. In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the written description rejections under 35 U.S.C. § 112.

Enablement

On pages 16-23 of the Office Action, claims 1-12, 29, 30 and 40-45 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. The Office acknowledges that the specification enables claims directed to X-ray diffraction-quality crystals of human LXRβ LBD consisting of the contiguous amino acid residues 220 to 461 of SEQ ID NO:1 complexed with T0901317 or GW3965, wherein the crystals have the space group and unit cell parameters specified.

Applicants note that claims 3-7 and 42, as amended herein, recite the particular combination of limitations indicated by the Office to be enabled by the instant specification, and therefore, should satisfy the enablement standard as applied by the Office.

The rejection as applied to the remaining pending claims is respectfully traversed. The Office has cited cites to the factors enumerated by *In re Wands* 858 F.2d 731, 737 (Fed. Cir. 1988) to support the proposition that the present claims are not enabled. In particular, the Office states that "the specification only describes 4 X-ray diffraction crystals (2 crystals with space group $P2_12_12_1$, 1 crystal with space group $P6_122$ and 1 crystal with space group $P2_12_12$) having the specific amino acid sequence, space group, unit cell dimension and bond angles as disclosed in pages 6 and 24, and Table 1". However, the Office states that "[i]n light of the notion that obtaining X-ray diffraction quality crystals is highly unpredictable" (citing to the previous enablement rejection), "the scope of crystals explained above [*e.g.*, having additional amino acid sequences attached] is not commensurate with the disclosure provided in the instant application…" (Office Action at pages 22-23).

Applicants clarify for the record that at least the following species of LXRβ LBD, in apo or complexed form, were successfully crystallized following the teaching of the specification as filed, namely, 2 species of crystals of LXRβ LBD complexed with T0901317 or GW3965 having space group $P2_12_12_1$ are disclosed in Table 1 of US 07/0060740; 2 species of crystals of LXRβ LBD in apo form or complexed with T0901317 having space group $P6_122$ are disclosed in paragraph 19 and 125, respectively, of US 07/0060740; 2 species of crystals of LXRβ LBD in apo form or complexed with the NR-box of TIF having space group $P2_12_12$ are disclosed in paragraphs 18 and 20, respectively, of US 07/0060740.

Each of the grounds raised by the Office in maintaining the position that the claims are not enabled is discussed in more detail below.

Claim breadth in relation to Applicants' disclosure

Applicants traverse the Office's maintained position that claims 8-10 (and claims dependent therefrom), which are directed to crystals of the LXRβ LBD, in apo- (unliganded) form or complexed to the particular ligand specified, having the **exact** space group and unit cell dimensions exemplified in the instant specification, *e.g.*, in paragraphs 18-20, respectively, of US 07/0060740, are not adequately enabled by the instant application. Similarly, dependent claims 3-7 and 42 are directed to crystals of the LXRβ LBD, in apo form or complexed to the particular ligand specified, that comprise or consist of the particular amino acid sequence of the LXRβ

LBD specified, and recite the **exact** space group and unit cell dimensions disclosed in the instant specification, e.g., in Table 1, paragraphs 125, 20 and 19, respectively, of US 07/0060740. Paragraphs 122-126 of US 07/0060740 describe experimental data with explanations on how to make and characterization of the claimed crystals. The crystallization conditions and methods disclosed in the specification resulted in crystals having the space group and parameters encompassed by claims 8-10 and 42. Applicants do not understand the Office's position in rejecting these claims since the Office admits that the specification discloses "4 X-ray diffraction crystals" with the particular structural parameters encompassed by the claims, and those particular working examples are specified by these claims.

Applicants also submit that claims 8-10 are commensurate in scope with exemplary claim 1 of case 4 of the Trilateral Report, which was deemed by the USPTO to satisfy the enablement requirement. More specifically, the Trilateral Report states that claims to a crystalline form of a polypeptide (e.g., like exemplary claim 1 of case 4) satisfy the enablement requirement, if the specification teaches how to make the claimed crystals and if one skilled in the art could use the claimed crystal without undue experimentation (see the Trilateral Report at page 67 and case 4 of the Trilateral Report at page 66). The instant specification discloses how to make the claimed compositions, *e.g.*, in paragraphs 122-126 of US 07/0060740, and one of skill in the art could have used the claimed crystal without undue experimentation.

It is also noted for the record that none of claims 1-10 or 40-42 requires "X-ray diffraction quality crystals," "for use to identify therapeutic compounds "for treatment of atherosclerosis," which the Office alleges are "highly unpredictable" to obtain, and that "one would have to painstakingly determine which of the genera of crystals as described above represent the biologically relevant 3-D structures so that structural studies can be performed in order to identify and synthesize new therapeutic compounds for treatment of atherosclerosis by inducing cholesterol efflux from macrophages/foam cells." (See Office Action at pages 22-23). Claims 1-10 and 40-42 are directed to crystals of LXRβ LBD, in apo form or complexed to the particular ligand specified, that comprise or consist of the particular amino acid sequence of the LXRβ LBD specified, and/or recite the exact space group and unit cell dimensions. Although Applicants reiterate that at least 6 X-ray-diffraction quality crystals were successfully obtained following the guidance provided in the instant specification (and thus, claims to x-ray quality

crystals are fully enabled by the specification), claims 1-10 or 40-42 encompass both x-ray and non-x-ray quality crystals, both forms of which are fully enabled by the instant application.

Similarly, the remaining claims are commensurate in scope with Applicants' disclosure. For example, claims 1 and 40 require the LXRβ LBD crystal to be complexed to a particular ligand and to have the space group specified (namely, $P2_12_12_1$, $P6_122$ and $P2_12_12$), in addition to the LXRβ LBD amino acid sequence specified. Claims 2 and 41 are directed to LXRβ LBD crystals having the structural parameters of the base claim, wherein the LXRβ LBD polypeptide sequence "consists of" the amino acid sequence disclosed in SEQ ID NO:1. Similarly, claims 29-30 and 43-45 require the LXRβ LBD crystal to be complexed to a particular ligand and to include the binding pocket having the structural coordinates of Table 2 within the deviation specified, in addition to the LXRβ LBD amino acid sequence specified. The genus of LXRβ LBD polypeptides encompassed by these crystal claims does not have substantial variation, since all must encode a polypeptide comprising, or consisting of, the amino acid sequence specified.

The specification teaches how to make the claimed crystals, for example in paragraphs 122-126 of US 07/0060740. The amino acid sequence and domain characterization of LXRβ LBD were known in the art at the time the instant application was filed and are described in the instant application. The structural coordinates of human LXRβ LBD, in complex form, were set forth in Table 2 of the application.

State of the Art / Level of predictability in the art

With respect to the state-of-the-art in generating LXRβ LBD polypeptides, techniques for generating LXRβ LBD polypeptides (and variants thereof) were known in the art and were performed routinely by molecular biologists at the time the present application was filed. The disclosure also describes and demonstrates methods for successfully crystallizing LXRβ LBD polypeptides. Once the crystallization conditions are established, one of ordinary skill in the art could have practiced the claimed invention (which, as discussed above, is directed to the very specific LXRβ LBD crystals generated following the conditions outlined in the specification), by routine experimentation. Therefore, Applicants submit that following the teachings of the specification, one of ordinary skill in the art would have been able to generate crystals of LXRβ

LBD polypeptide having the structural information encompassed by the claims by simply following the teachings of the specification.

Applicants previously cited Itoh, S. I. and M. A. Navia (1995) *Protein Science*, (4), 2261-2268 and Sauer, U. H., S. Dao-Pin, and B. W. Matthews (1992) *Journal of Biological Chemistry* (267) 2393-2399 as supporting the assertion that at the time the instant application was filed, it was known in the art that variants of proteins with known crystallization parameters were likely to readily crystallize with similar crystal structures as long as the variations introduced did not markedly affect intermolecular crystal contacts or amino acid residues important for protein stability (*i.e.*, within the hydrophobic core). Even mutations that had an effect in altering protein stability, such as inserting a proline amino acid, were found to crystallize with similar crystallization parameters as the native protein, emphasizing that well-folded proteins can exhibit crystallization properties similar to the non-mutated counterparts. Sauer, U. H., *supra*.

Applicants submit that the numerous reference cited by the Office in support of the alleged unpredictability of the crystallography art are not relevant to the present claims in view of their scope. Applicants are claiming the **particular** LXRβ LBD crystals that they prepared following the teachings in the specification. The application teaches how to make and use claimed crystals of LXRβ LBD polypeptides, e.g., crystals of LXRβ LBD polypeptides of 2 species of crystals of LXRβ LBD complexed with T0901317 or GW3965 having space group $P2_12_12_1$; 2 species of crystals of LXRβ LBD in apo form or complexed with T0901317 having space group $P6_122$; 2 species of crystals of LXRβ LBD in apo form or complexed with the NR-box of TIF having space group $P2_12_12$, and the reference sequence specified. Applicants had disclosed (and optimized) in the present application the crystallization conditions of the LXRβ LBD polypeptide within the scope of the present claims. In view of the disclosure of the specification and the knowledge in the field of protein crystallography at the filing date, undue experimentation would not be required to make and use the subject matter covered by the claims.

In view of the foregoing, Applicants, therefore, respectfully request reconsideration and withdrawal of the rejections of claims 1-12, 29, 30 and 40-45 under 35 U.S.C. § 112, first paragraph, for failure to satisfy the enablement requirement.

Applicants, therefore, respectfully request reconsideration and withdrawal of the rejection of claims 1-12, 29, 30 and 40-45 under 35 U.S.C. § 112, first paragraph, for lack of enablement and written description.

Rejection of Claims 1, 3, 11, 12, 29-32, 35, 43 and 45 under 35 U.S.C. § 102(e)

On pages 24-25 of the Office Action, the Office has rejected claims 1, 3, 11, 12, 29-32, 35, 43 and 45 under 35 U.S.C. §102(e) as allegedly being anticipated by Bledsoe *et al.* (US Patent Application No. 10/418,007, (effective filing date 04/26/2002)).

The Office has maintained this rejection because it has interpreted the transitional phrase "consisting essentially of" as an open-ended phrase, and therefore, under this interpretation the claims directed to the crystal complex of human LXRβ LBD polypeptide having the amino acid sequence specified and T0901317 would allegedly be anticipated by the disclosure in Bledsoe *et al.*

While Applicants do not concede to the Office's stated reasons for this rejection, this rejection has been met by amending the rejected claims to replace the objected phrase with "consisting of." The Bledsoe priority application discloses a fragment of human LXRβ LBD polypeptide from amino acid residues 214-462. The claims, as amended herein, are directed to the aforesaid crystal LXRβ LBD complexes, wherein the LXRβ LBD polypeptide consists of amino acids Leu220 to Glu461, or Gly213 to Glu461, of the LXRβ LBD polypeptide, which is shorter than the fragment disclosed in the Bledsoe application. Claims 29-30 and 43-45 are directed to crystal LXRβ LBD complexes defined by the amino acid sequences or the structural coordinates of Table 2 specified, within an RMSD of less than 1.5A. The structural coordinates of Table 2 were not taught or suggested by the Bledsoe priority application. Similarly, claim 43 requires the coordinates to be resolved using the structure of the thyroid hormone receptor as a search model, which again was not or suggested by the Bledsoe priority application.

In view of the foregoing, reconsideration and withdrawal of the rejection of claims 1, 3, 11, 12, 29-32, 35, 43 and 45 is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, reconsideration is respectfully requested. This application should now be in condition for allowance; a notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

A request for an extension of time and required fee are submitted herewith. If there is any additional fee occasioned by this response, including excess claim fees, that is not covered by the present submission, please charge any deficiency to Deposit Account No. 50-2762, referencing Attorney Docket No. W2025-7030US / AM101296US.

Respectfully submitted,
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